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**Subventricular spread of diffuse intrinsic pontine glioma.**

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**Public Summary:**

Diffuse intrinsic pontine glioma (DIPG) is the second most common malignant pediatric brain tumor and the leading cause of brain tumor death in childhood. Standard therapy consisting of local radiotherapy to a dosage of 54-60 Gy extends median survival from 5 to ~9 months; 5-year survival remains less than 1%. Here, we report an autopsy series of 16 patients evaluated from 2009–2014 at Stanford (n = 10) and VU (n = 6) University Medical Center. Consistent with previous reports, we found widespread dissemination of DIPG with extension to midbrain and medulla in 63%, cerebellum in 56%, thalamus in 56%, frontal cortex in 25% and supratentorial leptomeninges in 25%. The spinal cord was not consistently examined, but metastases were found in 2 of 3 cases examined; both had clinical evidence of spinal cord spread. A previously under-recognized pattern of subventricular spread was noted in 10/16 cases, with infiltration of the subventricular zone (SVZ) and tumor nodules in the frontal horns of the lateral ventricles. In three cases lateral ventricular disease was noted on pre-mortem MRI, but subclinical tumor invasion in the SVZ of the lateral ventricles was found in 6 additional cases; subventricular spread was found in the third ventricle of one additional case. The observed pattern of ventricular/subventricular involvement could be due to direct invasion along the SVZ corridor, intraventricular cerebrospinal fluid (CSF) seeding of the SVZ, or an as yet undescribed mechanism. The postnatal SVZ is a neural stem cell niche in the human brain and DIPG cells express an immunophenotype reminiscent of neural precursor cells. Whether DIPG cells exhibit a particular tropism for this niche remains to be explored. This study shows subventricular tumor spread in the majority of patients, typically later in the course of their disease. Thus as future therapies evolve to control local disease, strategies including extended or whole brain irradiation may become crucial. The patterns of widespread dissemination, including leptomeningeal, direct extension and subventricular spread, suggest that the extent of the optimal radiation field should be re-examined.

**Scientific Abstract:**

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